CLAIMS:

1. A composition for generating an immune response in a mammal, said composition comprising,

a polynucleotide component consisting essentially of one polynucleotide encoding an HIV immunogenic polypeptide derived from a first HIV strain, and

a polypeptide component comprising one or more HIV immunogenic polypeptides analogous to the polypeptide encoded by said polynucleotide component, with the proviso that at least one HIV immunogenic polypeptide of the polypeptide component is derived from a second HIV strain, wherein said first HIV strain and said second HIV strain are different.

2. A composition as in claim 1 wherein said second HIV strain is an HIV strain of the same subtype as said first HIV strain.

3. A composition as in claim 1 wherein said second HIV strain is an HIV strain of a different subtype than said first HIV strain.

4. A composition for generating an immune response in a mammal, said composition comprising,

a polynucleotide component comprising two or more polynucleotide sequences comprising coding sequences for two or more analogous HIV immunogenic polypeptides derived from different HIV strains, and

a polypeptide component comprising one or more HIV immunogenic polypeptides analogous to the polypeptide encoded by said polynucleotide component, with the proviso that, if the polypeptide component comprises the same number or greater than the number of analogous HIV immunogenic polypeptides encoded by the polynucleotide component, then at least one of the HIV immunogenic polypeptides of the polypeptide component is derived from a different HIV strain than the HIV immunogenic polypeptides provided by the polynucleotide component.

5. A composition as in claim 4 wherein said coding sequences for at least two of the HIV immunogenic polypeptides are derived from different HIV strains of the same subtype.

6. A composition as in claim 5 wherein said at least one HIV immunogenic polypeptides of the polypeptide component derived from a different HIV strain than the HIV immunogenic polypeptides provided by the polynucleotide component is derived from a different HIV strain of the same subtype as said HIV immunogenic polypeptides provided by the polynucleotide component.

7. A composition as in claim 4 wherein said coding sequences for at least two of the HIV immunogenic polypeptides are derived from different HIV strains of different subtypes.

8. A composition as in claim 7 wherein said at least one HIV immunogenic polypeptides of the polypeptide composition derived from a different HIV strain than the HIV immunogenic polypeptides provided by the polynucleotide component is derived from a different HIV strain of a different subtype from said HIV immunogenic polypeptides provided by the polynucleotide component.

9. A composition for generating an immune response in a mammal, said composition comprising,

a polynucleotide component consisting essentially of one polynucleotide encoding an HIV immunogenic polypeptide derived from a first HIV strain, and

a polypeptide component comprising one or more HIV immunogenic polypeptides analogous to the polypeptide encoded by said polynucleotide component, with the proviso that at least one HIV immunogenic polypeptide of the polypeptide component is derived from a second HIV strain, wherein said first HIV strain and said second HIV strain are different;

with the provisos that (i) the polynucleotide component does not encode an analogous HIV immunogenic polypeptide derived from any subtype other than the

first subtype, and (ii) the polypeptide component does not comprise an analogous HIV immunogenic polypeptide derived from any subtype other than the first subtype.

10. A composition for generating an immune response in a mammal, said composition comprising,

a polynucleotide component comprising two or more polynucleotide sequences comprising coding sequences for two or more analogous HIV immunogenic polypeptides derived from different HIV strains, and

a polypeptide component comprising one or more HIV immunogenic polypeptides analogous to the analogous polypeptides encoded by said polynucleotide component, with the proviso that at least one of the HIV immunogenic polypeptides of the polypeptide component is derived from a different HIV strain one of the analogous HIV immunogenic polypeptides provided by the polynucleotide component.

11. The composition of claim 10 wherein one or more of the analogous HIV immunogenic polypeptides are from different HIV subtypes.

12. The composition of any of claims 1 to 11, wherein said polynucleotide component or said polypeptide component comprises at least one polynucleotide that is a native polynucleotides or polypeptide.

13. The composition of any of claims 1 to 11, wherein said polynucleotide component comprises at least one polynucleotide that is a synthetic polynucleotide.

14. The composition of claim 13, wherein said synthetic polynucleotide comprises codons optimized for expression in mammalian cells.

15. The composition of claim 14, wherein said synthetic polynucleotide comprises codons optimized for expression in human cells.

16. The composition of any of claims 1 to 11, wherein the polynucleotide component encoding an HIV immunogenic polypeptide and the polypeptide component comprising an HIV immunogenic polypeptide are HIV envelope polypeptides.

17. The composition of claim 16, wherein at least one of said polynucleotide component encoding an HIV immunogenic polypeptide and saiad polynucleotide component comprising HIV immunogenic polypeptides comprises an alteration or a mutation.

18. The composition of claim 17 wherein said polynucleotides component encoding said HIV immunogenic polypeptide comprises an alteration or mutation.

19. The composition of claim 17 wherein said polypeptide HIV immunogenic polypeptide component comprises an alteration or mutation.

20. The composition of claim 18 or claim 19 which comprises a mutation in the cleavage site or a mutation in the glycosylation site.

21. The composition of claim 18 or claim 19 which comprises a deletion or modification of the V1 region.

22. The composition of claim 18 or claim 19 which comprises a deletion or modification of the V2 region.

23. The composition of claim 18 or claim 19 which comprises a deletion or modification of the V3 region.

24. The composition of claim 18 or claim 19 which comprises a deletion or modification of regions selected from the group consisting of the V1 region, the V2 region, the V3 region, and combinations thereof.

25. The composition of claim 18 or claim 19 which exposes a neutralizing epitope of an HIV env protein.

26. The composition of claim 25 wherein at least one of said envelope polypeptides is modified to expose a CD4 binding region or an envelope binding region that binds to a CCR5 chemokine co-receptor.

27. The composition of any of claims 1 to 11, wherein at least one polynucleotide encoding an HIV immunogenic polypeptide encodes an immunogenic HIV polypeptide selected from the group consisting of: Gag, Env, Pol, Prot, Int, RT, vif, vpr, vpu, tat, rev, and nef.

28. The composition of any of claims 1 to 11, wherein the first HIV subtype is selected from the group consisting of: subtype A, subtype B, subtype C, subtype D, subtype E, subtype F, subtype G, subtype H, subtype I, subtype J, subtype K, subtype N and subtype O.

29. The composition of any of claims 1 to 11, wherein at least one of said immunogenic HIV polypeptides comprises one or more alterations or mutations.

30. The composition of any of claims 1 to 11, wherein said polynucleotide component further comprises a sequence encoding an additional antigenic polypeptide, with the proviso that the additional antigenic polypeptide is not an immunogenic polypeptide derived from an HIV-1 strain.

31. The composition of claim 30, wherein said polypeptide component further comprises a polypeptide having an additional antigenic peptide, with the proviso that the additional antigenic polypeptide is not an immunogenic polypeptide derived from an HIV-1 strain.

32. The composition of any of claims 1 to 11, wherein said polynucleotide component further comprises sequences encoding one or more control elements compatible with expression in a selected host cell, wherein said control elements are operable linked to polynucleotides encoding HIV immunogenic polypeptides.

33. The composition of claim 32, wherein said control elements are selected from the group consisting of a transcription promoter, a transcription enhancer element, a transcription termination signal, polyadenylation sequences, sequences for optimization of initiation of translation, an internal ribosome entry site, and translation termination sequences.

34. The composition of claim 33, wherein said transcription promoter is selected from the group consisting of CMV, CMV+intron A, SV40, RSV, HIV-Ltr, MMLV-ltr, and metallothionein.

35. A method of generating an immune response in a subject, comprising,

providing a composition for generating an immune response in a mammal as in any of claims 1 to 34 and 74-82;

administering one or more gene delivery vectors comprising the polynucleotides of said polynucleotide component of the composition into said subject under conditions that are compatible with expression of said polynucleotides in said subject for the production of encoded HIV immunogenic polypeptides; and

administering the polypeptide component to said subject.

36. The method of claim 35, wherein said one or more gene delivery vectors and said polypeptide component are administered concurrently.

37. The method of claim 35, wherein said one or more gene delivery vectors and said polypeptide component are administered sequentially.

38. The method of claim 35, wherein said polypeptide component further comprises an adjuvant.

39. The method of claim 35, wherein said polynucleotide component further comprises a carrier.

40. The method of claim 35, wherein said one or more gene delivery vectors are nonviral vectors.

41. The method of claim 35, wherein said one or more gene delivery vectors are delivered using a particulate carrier.

42. The method of claim 35, wherein said one or more gene delivery vectors are coated on a gold or tungsten particle and said coated particle is delivered to said subject using a gene gun.

43. The method of claim 35, wherein said one or more gene delivery vectors are delivered using a PLG particle.

44. The method of claim 35, wherein said one or more gene delivery vectors are encapsulated in a liposome preparation.

45. The method of claim 44, wherein said one or more gene delivery vectors are viral vectors.

46. The method of claim 45, wherein said viral vectors are selected from the group consisting of different subtypes, species or serotypes of viral vectors.

47. The method of claim 46, wherein said viral vectors are retroviral vectors.

48. The method of claim 45, wherein said viral vector are lentiviral vectors.

49. The method of claim 45, wherein said viral vectors are alphaviral vectors.

50. The method of claim 45, wherein said viral vectors are adenoviral vectors.

51 . The method of claim 50 wherein said adenoviral vectors are live replicating vectors.

52 . The method of claim 50 wherein said adenoviral vectors are non-replicating vectors.

53. The method of claim 35, wherein said subject is a mammal.

54. The method of claim 53, wherein said mammal is a human.

55. The method of claim 35, wherein said immune response comprises an adaptive immune response.

56. The method of claim 55 wherein said immune response further comprises an innate immune response.

57. The method of claim 55 or claim 56 which comprises an Antibody Dependent Cell Mediated Cytotoxic response.

58. The method of claim 55 wherein said immune response comprises a humoral immune response.

59. The method of claim 55, wherein said immune response comprises a cellular immune response.

60. The method of claim 35, wherein said one or more gene delivery vectors are administered intramuscularly, intramucosally, intranasally, subcutaneously, intradermally, transdermally, intravaginally, intrarectally, orally or intravenously.

61. The method of claim 35, wherein said immune response results in generating neutralizing antibodies in the subject against multiple strains derived from the first HIV subtype.

62. The method of claim 35, wherein said immune response results in generating neutralizing antibodies in the subject against multiple strains derived from the more than one HIV subtype.

63. The method of claim 35 wherein said immune response comprises the in vivo generation in said subject of broadly neutralizing antibodies that neutralize multiple HIV isolates.

64. The method of claim 63 wherein said broadly neutralizing antibodies are characterized in that they demonstrate neutralizing activity to HIV strains utilizing the CCR5 coreceptor.

65. The method of claim 63 wherein said broadly neutralizing antibodies are characterized in that they demonstrate neutralizing activity against two or more HIV strains from the same HIV subtype.

66. The method of claim 65 wherein said neutralizing antibodies demonstrate neutralizing activity against two or more HIV strains selected from the group consisting of the following HIV isolates: Bal, JR-FL; Bx08; 6101; 692; 1168; 1196; and ADA.

67. The method of claim 63 wherein said broadly neutralizing antibodies are characterized in that they demonstrate neutralizing activity against two or more HIV strains from two or more different HIV subtypes.

68. The method of claim 67 wherein said neutralizing antibodies demonstrate neutralizing activity against two or more HIV subtypes selected from the group consisting of the following HIV subtypes: A, B, C, D, E, F, G, and O.

69. The method of claim 35 wherein said immune response comprises the generation in said subject of antibodies that mediate Antibody Dependent Cell Mediated Cytotoxicity (ADCC).

70. The method of claim 69 wherein said antibodies are characterized in that they demonstrate ADCC activity against two or more HIV strains from two or more different HIV subtypes.

71. The method of claim 70 wherein said antibodies demonstrate ADCC activity against two or more HIV subtypes selected from the group consisting of the following HIV subtypes: A, B, C, D, E, F, G, and O.

72. The method of claim 69 wherein said broadly neutralizing antibodies are characterized in that they demonstrate neutralizing activity against two or more HIV strains from the same HIV subtype.

73. The method of claim 69 wherein said neutralizing antibodies demonstrate neutralizing activity against two or more HIV strains selected from the group consisting of the following HIV isolates: Bal, JR-FL; Bx08; 6101; 692; 1168; 1196; and ADA.

74. A composition for generating an immune response in a mammal as in any of claims 1-34, wherein said polypeptide component may be administered in the form of a polynucleotide expressing said polypeptide component.

75. A composition as in claim 74 wherein said polypeptide component is administered with a viral vector.

76. A composition as in claim 75 wherein said viral vector is selected from the group consisting of adenovirus, alphavirus and pox virus.

77. A composition for generating an immune response in a mammal as in claim 74, wherein one or more of said polynucleotides are administered to a subject as a DNA formulation.

78. A composition as in claim 68 wherein said DNA formulation comprises DNA and PLG.

79. A composition as in any of claims 1-34 wherein said polypeptide component is administered in the form of a protein expressed on a virus like particle.

80. A composition for generating an immune response in a mammal, said composition comprising,

a polynucleotide component comprising a polynucleotide encoding an HIV immunogenic polypeptide derived from a first HIV strain, and

a polypeptide component comprising an HIV immunogenic polypeptide analogous to the polypeptide encoded by said polynucleotide component, with the proviso that at least one HIV immunogenic polypeptide of the polypeptide component is derived from a second HIV strain, wherein said first HIV strain and said second HIV strain are different.

81. A composition as in claim 80 wherein said second HIV strain is an HIV strain of the same subtype as said first HIV strain.

82. A composition as in claim 81 wherein said second HIV strain is an HIV strain of a different subtype than said first HIV strain.

83. A method as in any of claims 35-73 wherein said polypepetide component is delivered by a viral vector.